

DEAV2003/0002 US NP
Application No. 10/751,545

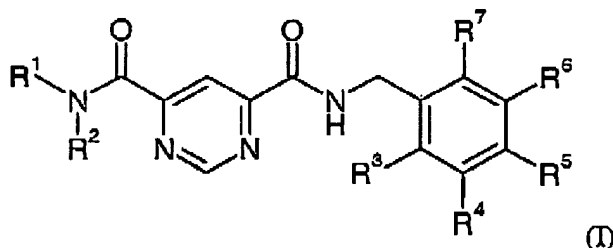
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Amendments to the Claims

This listing of claims will replace all prior versions and listings of claims in the application.

Listing of Claims

1. (Currently amended) A compound of formula I



wherein

R¹ is

hydrogen atom or $-(C_1-C_6)$ -alkyl,

R² is

$-(C_1-C_6)$ -alkyl that is substituted, once, twice or three times, by

$-C(O)-O-R^8$,

$-(C_1-C_6)$ -alkyl- $O-R^8$,

$-(C_6-C_{14})$ -aryl that is substituted, once, twice or three times, independently of each other, by R¹¹, or

~~Het that is a saturated or unsaturated monocyclic or bicyclic, 3 to 10 membered heterocyclic ring system which contains 1, 2 or 3 identical or different ring heteroatoms selected from the group consisting of nitrogen, oxygen and sulfur and is unsubstituted or substituted, once or more than once, by R¹³;~~

Het, wherein Het is selected from the group consisting of azepine, azetidine, aziridine, benzimidazole, benzofuran, 4H-benzo[1,4]oxazine, benzoxazole, benzothiazole, benzo[thiophene, quinoxaline, quinoline, quinoxaline, chroman, cinnoline, oxirane, 1,2-diazepine, 1,3-diazepine, 1,4-diazepine, 1,4-dioxin, dioxole, furan, imidazole, indazole, indole,

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isoquinoline, isochroman, isoindole, isoxazole, isothiazole, 1,2-oxazine, 1,3-oxazine, 1,4-oxazine, oxazole, phthalazine, piperidine, pyran, pyrazine, pyrazole, pyridazine, pyridine, pyrimidine, pyridoimidazole, pyridopyridine, pyridopyrimidine, pyrrol, tetrazole, 1,2-thiazine, 1,3-thiazine, 1,4-thiazine, thiazole, thiophene, thiopyran, 1,2,3-triazine, 1,2,4-triazine, 1,3,5-triazine, 1,2,3-triazole, and 1,2,4-triazole, and wherein Het is unsubstituted or substituted, once, twice or three times, independently of each other, by R¹³,

R³, R⁴, R⁵, R⁶ and R⁷ are identical or different and are, independently of each other,

hydrogen,

halogen,

-(C₁-C₆)-alkyl, in which alkyl is unsubstituted or substituted, once, twice or three times,
by halogen,

-O-(C₁-C₆)-alkyl, in which alkyl is unsubstituted or substituted, once, twice or three
times, by halogen, or

-S-(C₁-C₆)-alkyl,

R⁸ is

hydrogen atom, or

-(C₁-C₆)-alkyl,

R¹¹ is

-(C₂-C₆)-alkyl-C(O)-O-R⁸,

-O-(C₁-C₆)-alkyl-C(O)-O-R⁸,

-NR¹⁴R¹⁵,

-(CH₂)_k-NR⁹R¹⁰,

-O-(C₂-C₆)-alkyl-NR⁹R¹⁰, or

-NR⁸-C(O)-(C₁-C₆)-alkyl, in which alkyl is unsubstituted or substituted, once, twice or
three times, by R¹²,

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R^9 and R^{10} are identical or different and are, independently of each other,

hydrogen atom, or

-(C₁-C₆)-alkyl, or

taken together with the nitrogen atom to which they are attached form a 5-, 6- or 7-

membered saturated azaheterocyclyl ring wherein one or two further carbon atoms

thereof are optionally replaced by a heteroatom that is an oxygen, sulfur or nitrogen atom,

and wherein the nitrogen atom is optionally unsubstituted or substituted by (C₁-C₆)-alkyl,

k is

2, 3, 4 or 5,

R^{12} is

halogen,

cyano,

nitro,

hydroxyl,

amino,

-C(O)-O-(C₁-C₆)-alkyl, or

-C(O)-OH,

R^{13} is

halogen,

cyano,

nitro,

hydroxyl,

amino,

-C(O)-O-(C₁-C₆)-alkyl,

-C(O)-OH,

-(C₁-C₆)-alkyl that is unsubstituted or substituted, once, twice or three times, by halogen,

-O-(C₁-C₆)-alkyl, where alkyl is unsubstituted or substituted, once, twice or three times,

by halogen,

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pyridyl, or

phenyl that is unsubstituted or substituted, once or more than once and independently of each other, by a radical from the series halogen, (C₁-C₆)-alkoxy and (C₁-C₆)-alkyl, and

R¹⁴ and R¹⁵ together with the nitrogen atom to which they are attached form

a 5-, 6- or 7-membered saturated azaheterocyclyl ring wherein one or two further carbon atoms thereof are optionally replaced by a heteroatom that is oxygen, sulfur or nitrogen, and wherein each nitrogen atom thereof is optionally independently unsubstituted or substituted by (C₁-C₆)-alkyl, or

a stereoisomer thereof, a mixture of stereoisomers thereof in any ratio, or a physiologically tolerable salt thereof.

2. (Currently amended) The compound according to claim 1, wherein

R² is

-(C₁-C₄)-alkyl, where alkyl is substituted, once, twice or three times, by

-C(O)-O-R⁸,

-(C₁-C₄)-alkyl-O-R⁸,

phenyl that is substituted, once, twice or three times, independently of each other, by R¹¹, or

Het, wherein Het is selected from the group consisting of that is azepine,

azetidine, aziridine, benzimidazole, benzo[1,4]dioxin, 1,3-benzodioxole, benzofuran, 4H-benzo[1,4]oxazine, benzoxazole, benzothiazole, benzothiophene, quinazoline, quinoline, quinoxaline, chroman, cinnoline, oxirane, 1,2-diazepine, 1,3-diazepine, 1,4-diazepine, 1,4-dioxin, dioxole, furan, imidazole, indazole, indole, isoquinoline, isochroman, isoindole, isoxazole, isothiazole, 1,2-oxazine, 1,3-oxazine, 1,4-oxazine, oxazole, phthalazine, piperidine, pyran, pyrazine, pyrazole, pyridazine, pyridine, pyrimidine, pyridoimidazole, pyridopyridine, pyridopyrimidine, pyrrol, tetrazole, 1,2-thiazine, 1,3-thiazine, 1,4-thiazine, thiazole, thiophene,

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thiopyran, 1,2,3-triazine, 1,2,4-triazine, 1,3,5-triazine, 1,2,3-triazole, and
~~or~~ 1,2,4-triazole, and wherein Het is unsubstituted or substituted, once,
twice or three times, independently of each other, by R¹³.

R³, R⁴, R⁵, R⁶ and R⁷ are identical or different and are

hydrogen atom,

halogen,

-(C₁-C₆)-alkyl, in which alkyl is unsubstituted or substituted, once, twice or three times,
by halogen, or

-O-(C₁-C₆)-alkyl, in which alkyl is unsubstituted or substituted, once, twice or three
times, by halogen,

R⁸ is

hydrogen atom, or

-(C₁-C₄)-alkyl,

R¹¹ is

-(C₂-C₄)-alkyl-C(O)-O-R⁸,

-O-(C₁-C₄)-alkyl-C(O)-O-R⁸,

-N R¹⁴R¹⁵, wherein R¹⁴ and R¹⁵ taken together with the nitrogen atom to which they are
attached form imidazolidine, isothiazolidine, isoxazolidine, morpholine,
piperazine, piperidine, pyrazine, pyrazolidine, pyrrolidine, tetrazine or
thiomorpholine, and wherein each nitrogen atom thereof is optionally
independently unsubstituted or substituted by (C₁-C₄)-alkyl,

-(CH₂)_k-N R⁹R¹⁰,

-O-(C₂-C₄)-alkyl-NR⁹R¹⁰, or

-NH-C(O)-(C₁-C₄)-alkyl, wherein the alkyl is unsubstituted or substituted, once, twice or
three times, by R¹²,

R⁹ and R¹⁰ are identical or different and are, independently of each other,

hydrogen atom, or

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-(C₁-C₄)-alkyl, or
taken together with the nitrogen atom to which they are attached form imidazolidine,
isothiazolidine, isoxazolidine, morpholine, piperazine, piperidine, pyrazine, pyrazolidine,
pyrrolidine, tetrazine or thiomorpholine, and wherein the nitrogen atom is optionally
unsubstituted or substituted by -(C₁-C₄)-alkyl,

k is

2, 3 or 4, and

R¹³ is

halogen,
amino,
-C(O)-O-(C₁-C₄)-alkyl,
-C(O)-OH,
-(C₁-C₆)-alkyl that is unsubstituted or substituted, once, twice or three times, by halogen,
-O-(C₁-C₆)-alkyl, wherein the alkyl is unsubstituted or substituted, once, twice or three
times, by halogen,
pyridyl, or
phenyl that is unsubstituted or substituted, once or more than once and independently of
each other, by a radical from the series halogen, -(C₁-C₄)-alkoxy and -(C₁-C₄)-
alkyl.

3. (Currently Amended) The compound according to claim 1, wherein

R¹ is

hydrogen,

R² is

-(C₁-C₂)-alkyl that is substituted, once, twice or three times, by
phenyl that is substituted, once, twice or three times, independently of each other,
by R¹¹, or

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Het, ~~wherein Het is selected from the group consisting of~~ ~~that is~~ furan, imidazole, isothiazole, isoxazole, oxazole, pyrazole, pyridazine, pyridine, pyrimidine, pyrrole, thiazole, thiophene, 1,2,3-triazole, and ~~or~~ 1,2,4-triazole, and wherein Het is unsubstituted or substituted, once, twice or three times, independently of each other, by R¹³,

R³, R⁴, R⁵, R⁶ and R⁷ are identical or different and are, independently of each other,

hydrogen,

halogen,

methyl,

trifluoromethyl,

methoxy, or

trifluoromethoxy,

R⁸ is

hydrogen atom, or

-(C₁-C₄)-alkyl,

R¹¹ is

-(C₂-C₄)-alkyl-C(O)-O-R⁸,

-O-(C₁-C₄)-alkyl-C(O)-O-R⁸,

-N R¹⁴R¹⁵, wherein R¹⁴ and R¹⁵ taken together with the nitrogen atom to which they are attached form imidazolidine, isothiazolidine, isoxazolidine, morpholine, piperazine, piperidine, pyrazine, pyrazolidine, pyrrolidine, tetrazine or thiomorpholine, and wherein each nitrogen atom thereof is optionally independently unsubstituted or substituted by (C₁-C₄)-alkyl,

-(CH₂)_k-N R⁹R¹⁰,

-O-(C₂-C₄)-alkyl-NR⁹R¹⁰, or

-NH-C(O)-(C₁-C₄)-alkyl, wherein the alkyl is unsubstituted or substituted, once, twice or three times, by R¹²,

R⁹ and R¹⁰ are identical or different and are, independently of each other,

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hydrogen atom, or
-(C₁-C₄)-alkyl, or
taken together with the nitrogen atom to which they are attached form imidazolidine, isothiazolidine, isoxazolidine, morpholine, piperazine, piperidine, pyrazine, pyrazolidine, pyrrolidine, tetrazine or thiomorpholine, and wherein the nitrogen atom is optionally unsubstituted or substituted by -(C₁-C₄)-alkyl,

k is

2, 3 or 4,

R¹² is

halogen,
-C(O)-O-(C₁-C₄)-alkyl, or
-C(O)-OH, and

R¹³ is

halogen,
amino,
-C(O)-O-(C₁-C₄)-alkyl,
-C(O)-OH,
-(C₁-C₄)-alkyl that is unsubstituted or substituted, once, twice or three times, by halogen,
-O-(C₁-C₄)-alkyl, wherein the alkyl is unsubstituted or substituted, once, twice or three times, by halogen,
pyridyl, or
phenyl that is unsubstituted or substituted, once or more than once and independently of each other, by a radical from the series halogen, -(C₁-C₄)-alkoxy and -(C₁-C₄)-alkyl.

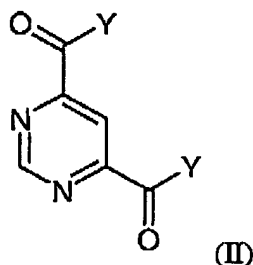
4. (Currently amended) A method for the ~~prophylaxis or therapy~~treatment of a patient having or subject to a disease whose course involves a detrimental increase in the activity of matrix metalloproteinase 13, wherein said disease is osteoarthroses, comprising

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administering to said patient a therapeutically effective amount of a compound according to claim 1.

5. (Currently amended) A method for the ~~prophylaxis or therapy~~ treatment of a patient having or subject to a disease whose course involves a detrimental increase in the activity of matrix metalloproteinase 13, wherein said disease is osteoarthroses, comprising administering to said patient a therapeutically effective amount of a compound according to claim 2.
6. (Currently amended) A method for the ~~prophylaxis or therapy~~ treatment of a patient having or subject to a disease whose course involves a detrimental increase in the activity of matrix metalloproteinase 13, wherein said disease is osteoarthroses, comprising administering to said patient a therapeutically effective amount of a compound according to claim 3.
7. (Original) A process for preparing the compound of formula I according to claim 1, comprising
- a) reacting a compound of formula II



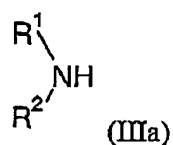
wherein Y is

halogen, hydroxyl or C₁-C₄-alkoxy, or forms, together with the carbonyl group, an active ester or a mixed anhydride,

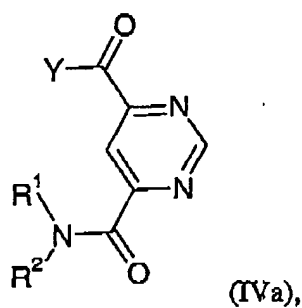
with a compound of formula IIIa

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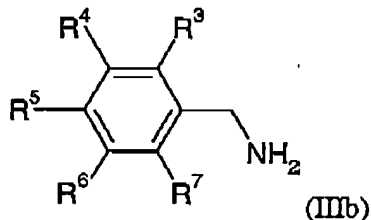
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wherein R^1 and R^2 , have the meanings given in the compound of formula I,
to form a compound of formula IVa



b) reacting the compound of formula IVa with a compound of formula IIIb



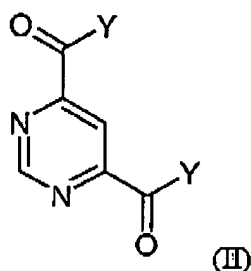
wherein R^3 , R^4 , R^5 , R^6 and R^7 have the meanings given in the compound of formula I, to
form the compound of formula I.

8. (Original) A process for preparing the compound of formula I according to claim 1,
comprising

a) reacting a compound of formula II

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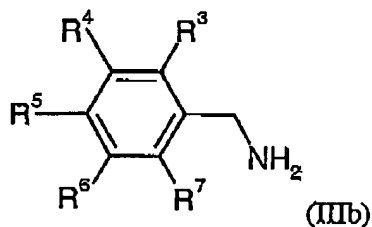
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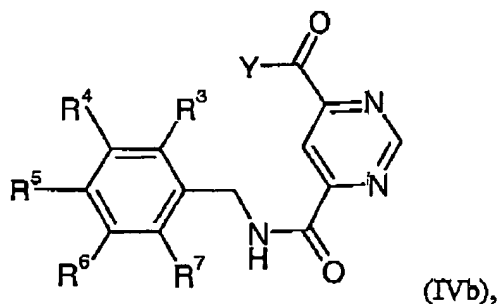
wherein Y is

halogen, hydroxyl or $\text{C}_1\text{-C}_4$ -alkoxy, or forms, together with the carbonyl group, an active ester or a mixed anhydride,

with a compound of formula IIIb



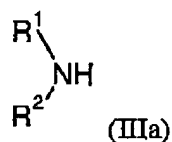
wherein R^3 , R^4 , R^5 , R^6 and R^7 have the meanings given in the compound of formula I, to form a compound of formula IVb



b) reacting the compound of formula IVb with a compound of formula IIIa

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wherein R^1 and R^2 , have the meanings given in the compound of formula I,
to form the compound of formula I.

9. (Original) A pharmaceutical preparation comprising a pharmaceutically effective amount of at least one compound of formula I according to claim 1 and a pharmaceutically suitable and physiologically tolerated carrier.

10-11. (Canceled)